REMARKS

As an initial matter, Applicant would like to thank the Examiner for conducting a telephone interview with the Applicant's representative on November 4, 2005. During the interview, the Election/Restriction Requirement made on June 3, 2003 was discussed. It was suggested that the Applicant amend the claims to include the elected species made on November 3, 2003. Further, the Examiner indicated that the Applicants should provide specific support recited in the specification directed to the amended claims. The Examiner also indicated that arguments as to why the amended claims are patentable in view of the prior art references cited in the Office Action should be presented when submitting the amended claims.

In response to the Official Action dated September 8, 2005, Applicant respectfully submits the present Amendment and Remarks.

Amendment to Claims

Claims 21 to 40 are currently pending in this application. Independent claims 21, 23, 28, and 32 have been amended in order to more distinctly claim various embodiments of the invention. In accordance to the election of restriction and election made on November 3, 2003 to the Election/Restriction Requirment dated June 3, 2003, these independent claims have been amended to recite the elected species "wherein the antibody is specific for cellular receptor and the peptide is a specific binding site derived from a natural ligand for a specific cellular receptor; and wherein the antibody is a murine anti-idiotype antibody 3H1 and the peptide is a complement fragment C3d." Further, these independent claims have also amended to clarify that the peptide is a peptide of SEQ ID NO: 1. Support for this can be

found throughout the specification, particularly at page 15 of the specification. No new matter has been added. These claims do not require additional searches from the Examiner, and thus Applicant respectfully request that they be entered.

Summary of the Office Action

In the Office Action, claims 21-40 are objected to under 37 CFR 1.821 (d) because a SEQ ID NO: is required. The Examiner has maintained the rejection of claims 21-40 under 35 U.S.C. §112, first paragraph, alleging that the subject matter thereof does not enable a person skilled in the art to make and use the invention commensurate in scope with the claims when the specification is only enabled for "a fusion protein comprising an anti-idiotypic anti-CEA antibody fused to a peptide consisting of SEQ ID NO: 1." The Examiner alleges that it would require undue experimentation for one skilled in the art to practice the invention as claimed since the specification discloses "only anti-idiotypic antibody 3H1 that induces anti-CEA antibody fused to a peptide consisting of SEQ ID NO: 1." The Examiner also alleges that there is insufficient guidance to the structure of the claimed peptide in the specification. Allegation that that there is "lack of guidance and working example to demonstrate that antibody comprises either light chain or heavy chain is capable of binding to any antigen" is also made in the Office Action.

The Examiner has also maintained the rejection of claims 21-40 under 35 U.S.C. §112, first paragraph, alleging that the subject matter thereof does not convey that the inventor had possession of the claimed invention at the time the application was filed. The Examiner further alleges that the specification does not provide an

adequate written description of the claimed invention for the same reasons in making the §112, first paragraph rejection above.

The Examiner has also rejected claims 29 and 37-40 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner alleges that claims 29 and 37-40 are ambiguous because one of ordinary skill in the art cannot appraise the metes and bound of the claimed amino acid sequence of the human C3d containing residues 1217-1232 without reference to a specific sequence.

The Examiner also alleges that this application is only entitled to the filing date of May 21, 2001 and not its parent application, 09/070,907 filed May 4, 1998, issued as USPN 6,238,667 (the '667 patent) and claims priority to Provisional Application No. 60/059,515 filed September 19, 1997.

In addition, the Examiner has also made a number of rejections under 35 U.S.C. §102. The Examiner has rejected claims 21-28 and 30-35 under 35 U.S.C. §102(b), alleging that the claimed subject matter is anticipated by WO 96/17625. The Examiner has rejected claims 32 and 33 under 35 USC Section 102 for being anticipated by Gerstmayer et al. (J Immunology 158:4584-4590, May 1997). The Examiner has rejected claim 28 under 35 USC Section 102 for being anticipated by U.S. Patent No. 5,314, 995 (May 1994). The Examiner has rejected claims 28 and 31 under 35 USC Section 102 for being anticipated by U.S. Patent No. 5,698,679.

Finally, the Examiner has rejected claims 21-22, 29, 32, 33, and 36-40 under 35 USC Section 103 for being unpatentable over WO 96/17625 (June 13, 1996) in

view of Lambris et al. (Proc Nat' Acad Sci 82:4235-4239, June 1985) and Dawa et al. (Dev Biol Stand 92: 3-11, 1998).

RESPONSE

Objection under 35 USC §112, first paragraph

The Examiner has made an objection to claims 21-40 under 37 CFR 1.821 (d). The Examiner alleges that a SEQ ID NO: is required in these claims. Applicant respectfully points out that all the independent claims have been amended to recite "a peptide of SEQ ID NO: 1" as required by the Examiner. Accordingly, this objection has been obviated.

First rejection under 35 USC §112, first paragraph

As discussed above, the Examiner has maintained the rejection of claims 21-40 under 35 U.S.C. §112, alleging that the subject matter thereof does not enable a person skilled in the art to make and use the invention commensurate in scope with the claims when the specification is only enabled for "a fusion protein comprising an anti-idiotypic anti-CEA antibody fused to a peptide consisting of SEQ ID NO: 1."

The Examiner further alleges that it would require undue experimentation for one skilled in the art to practice the invention as claimed since the specification discloses "only anti-idiotypic antibody 3H1 that induces anti-CEA antibody fused to a peptide consisting of SEQ ID NO: 1." The Examiner also alleges that there is insufficient guidance to the structure of the claimed peptide in the specification. Allegation that that there is "lack of guidance and working example to demonstrate that antibody comprises either light chain or heavy chain is capable of binding to any

antigen" is also made in the Office Action. Applicant respectfully points out that all the independent claims have been amended to recite a peptide consisting of SEQ ID NO: 1. Accordingly, this rejection has been obviated.

The invention as presently claimed is directed to an antigen-binding fusion protein comprising an antibody and a peptide possessing homophilic, immuno-stimulatory and/or membrane transport activities. Applicant respectfully points out that the present invention is a fusion protein comprising an anti-idiotypic anti-CEA antibody fused to a peptide of SEQ ID NO: 1 derived from the C3d region 1217-1232.

Hence, Applicant respectfully submits that the specification provides the necessary guidance to apply the claimed invention. The specification of the invention clearly provides an enabling disclosure for one of skill in the art to make the claimed fusion protein.

As the specification is fully supportive of the invention as presently claimed, Applicant respectfully requests the Examiner reconsider and withdraw this rejection under 35 USC §112, first paragraph.

Second rejection under 35 USC §112, first paragraph

As discussed above, the Examiner has maintained the rejection of claims 21-40 under 35 U.S.C. §112, alleging that the subject matter thereof does not convey that the inventor had possession of the claimed invention at the time the application was filed. The Examiner further alleges that the specification does not provide an adequate written description of the claimed invention for the same reasons in making the §112, first paragraph rejection above.

Again, Applicant respectfully points out that all the independent claims have been amended to recite a peptide consisting of SEQ ID NO: 1. Also as discussed in detailed above, the invention as presently claimed features fusion proteins which, in various embodiments of the invention, comprise an antibody and a peptide of SEQ ID NO: 1 comprising homophilic, immuno-stumulatory and/or membrane transport activity. Description of each of these embodiments of the invention is provided in the specification as filed (including the references incorporated therein), particularly in the examples.

Applicant respectfully submits that the application as filed fully describes and exemplifies the claimed invention, particularly in the examples. Hence, there can be no doubt that Applicant had possession of the claimed invention at the time the application was filed.

Applicant respectfully submits that the invention as presently claimed is more than adequately and definitely described in the application as originally filed. Applicant thus respectfully requests the Examiner to reconsider and withdraw this rejection.

Rejection under 35 USC §112, second paragraph

The Examiner has also rejected claims 29 and 37-40 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner alleges that claims 29 and 37-40 are ambiguous because one of ordinary skill in the art cannot appraise the metes and bound of the claimed amino acid sequence of the human C3d containing residues 1217-1232 without reference to a specific sequence.

Again, Applicant respectfully points out that all the independent claims have been amended to recite a peptide consisting of SEQ ID NO: 1. Accordingly, this rejection has been obviated.

Applicant respectfully submits that the invention as presently claimed is more than adequately and definitely described in the application as originally filed. Applicant thus respectfully requests the Examiner to reconsider and withdraw this rejection.

Priority Date

In the Office Action, the Examiner alleges that this application is only entitled to the filing date of May 21, 2001 and not its parent application, 09/070,907 filed May 4, 1998, issued as USPN 6,238,667 (the '667 patent) and claims priority to Provisional Application No. 60/059,515 filed September 19, 1997.

Specifically, the Examiner alleges that the '667 patent "is drawn only to a method of affinity *cross-linking* a peptide to an antibody by photo-chemically activating an azido compound, and thus does not support the claimed limitations [directed to] an antigen-binding *fusion protein* comprising an antibody and a peptide having a homophilic activity of the instant application."

Applicant respectfully points out that although the claims of the '667 patent are directed to methods of affinity cross-linking a peptide to an antibody and compositions thereof, the specification of this patent also recites fusion proteins of peptides incorporated into antibodies. Peptides of this patent include C3d peptides, signal peptides, antigenic peptides, peptides from self-binding locus of antibodies, peptide-conjugated antibodies, peptides cross-linked antibodies, and peptides bound

to any antibody including antibodies which are specific for cellular receptor and can transport across membrane structure. See column 1, lines 14-21, column 3, lines 58-62, column 6, lines 5-39, column 12, lines 32-56, column 14, lines 13-32, and examples 1-5 of this patent. Further, the specification of US Provisional Application 60/059,515 recites methods of affinity cross-linking peptides to antibodies and fusion proteins of peptides and antibodies. Accordingly, this application is entitled to the priority date of US Provisional Application 60/059,515.

First rejection under 35 USC §102 (b)

In the Office Action, the Examiner has rejected claims 21-28 and 30-35 under 35 USC Section 102 for being anticipated by WO 96/17625 (June 13, 1996). The Examiner alleges that this publication teaches a fusion protein comprising an antibody and a peptide, wherein the antibody can be a single chain scFv antibody or an antibody to CD21 or DC19, and wherein the peptide can be a C3d.

Applicant respectfully points out that independent claims have been amended to recite the elected species "wherein the antibody is specific for cellular receptor and the peptide is a specific binding site derived from a natural ligand for a specific cellular receptor; and wherein the antibody is a murine anti-idiotype antibody 3H1 and the peptide is a complement fragment C3d." Further, these independent claims have also amended to clarify that the peptide is a peptide of SEQ ID NO: 1.

Applicant respectfully submits that the cited document fails to disclose an antigen-binding fusion protein comprising (1) an antibody and (2) a peptide of SEQ ID NO: 1. This cited document neither teaches nor discloses fusion protein comprising (1) an antibody and (2) a peptide of SEQ ID NO: 1; wherein the antibody

is specific for cellular receptor and the peptide is a specific binding site derived from a natural ligand for a specific cellular receptor; and wherein the antibody is a murine anti-idiotype antibody 3H1 and the peptide is a complement fragment C3d.

Accordingly, Applicant respectfully requests that is rejection be withdrawn.

Second rejection under 35 USC §102 (b)

In the Office Action, the Examiner has rejected claims 32 and 33 under 35 USC Section 102 for being anticipated by Gerstmayer et al. (J Immunology 158:4584-4590, May 1997). The Examiner alleges that this publication teaches a fusion protein comprising (1) an antibody, which includes a single chain antibody scFv (FRP5) binding to erbB2; and (2) a peptide, which includes a fragment of B7-2225 having a membrane transport activity.

Again, Applicants respectfully points out that the pending claims are drawn to a fusion protein comprising a murine anti-idiotype antibody 3H1 and a peptide that is a complement fragment C3d, which is not disclosed in this publication. Further, this cited document neither teaches nor discloses fusion protein comprising (1) an antibody and (2) a peptide of SEQ ID NO: 1; wherein the antibody is specific for cellular receptor and the peptide is a specific binding site derived from a natural ligand for a specific cellular receptor; and wherein the antibody is a murine anti-idiotype antibody 3H1 and the peptide is a complement fragment C3d. Applicants also respectfully points out that the claimed priority date of this application predates this publication.

Accordingly, Applicant respectfully requests that is rejection be withdrawn.

Third rejection under 35 USC §102 (b)

In the Office Action, the Examiner has rejected claim 28 under 35 USC Section 102 for being anticipated by U.S. Patent No. 5,314,995 (May 1994). The Examiner alleges that this patent teaches a fusion protein made up of (1) an antibody, such as antigen L6; and (2) a peptide, such as IL-2 and IL6 having immunostimulatory activity.

Applicant respectfully points out that the antigen-binding fusion of claim 28 is clearly different from the fusion protein of this document. This claim is drawn to a fusion protein comprising a murine anti-idiotype antibody 3H1 and a peptide that is a complement fragment C3d, which is not disclosed in this patent. This cited document neither teaches nor discloses fusion protein comprising (1) an antibody and (2) a peptide of SEQ ID NO: 1; wherein the antibody is specific for cellular receptor and the peptide is a specific binding site derived from a natural ligand for a specific cellular receptor; and wherein the antibody is a murine anti-idiotype antibody 3H1 and the peptide is a complement fragment C3d. There is nothing in this document that teaches or suggests An antigen-binding fusion protein comprising (1) an antibody and (2) a peptide of SEQ ID NO: 1, having immuno-stimulatory activity, wherein said peptide does not interfere with antigen binding, and wherein said antibody comprises a light chain or heavy chain immunoglobulin molecule and wherein said peptide is attached to the C-terminal or the N-terminal of said light chain or heavy chain immunoglobulin molecule. Applicants also respectfully points out that the claimed priority date of this application predates this publication.

Accordingly, Applicant respectfully requests that is rejection be withdrawn.

Fourth rejection under 35 USC §102 (b)

In the Office Action, the Examiner has rejected claims 28 and 31 under 35 USC Section 102 for being anticipated by U.S. Patent No. 5,698,679 (December 1997). The Examiner alleges that this patent teaches a fusion protein comprising (1) an antibody that binds to a cellular receptor such as CD40 on normal cell such as APC cells and B cells; and (2) an immunogenic peptide such as ovalbumin 326-337.

This patent does not disclose our claimed fusion protein comprising a murine anti-idiotype antibody 3H1 and a peptide that is a complement fragment C3d.

Applicant respectfully submits that the antigen-binding fusion of amended claims 28 and 31 are clearly different from the fusion protein of this document. This cited document fails to disclose an antigen-binding fusion protein comprising (1) an antibody and (2) a peptide of SEQ ID NO: 1. This cited document neither teaches nor discloses fusion protein comprising (1) an antibody and (2) a peptide of SEQ ID NO: 1; wherein the antibody is specific for cellular receptor and the peptide is a specific binding site derived from a natural ligand for a specific cellular receptor; and wherein the antibody is a murine anti-idiotype antibody 3H1 and the peptide is a complement fragment C3d. Applicants also respectfully points out that the claimed priority date of this application predates this publication.

Accordingly, Applicant respectfully requests that is rejection be withdrawn.

Rejection under 35 USC §103 (a)

In the Office Action, the Examiner has rejected claims 21-22, 29, 32, 33, and 36-40 under 35 USC Section 103 for being unpatentable over WO 96/17625 (June

13, 1996) in view of Lambris et al. (Proc Nat' Acad Sci 82:4235-4239, June 1985) and Dawa et al. (Dev Biol Stand 92: 3-11, 1998).

As discussed above, WO 96/17625 teaches a fusion protein comprising an antibody and a peptide, wherein the antibody can be a single chain scFv antibody or an antibody to CD21 or DC19, and wherein the peptide can be a C3d.

With regard to the Lambris publication, the Examiner alleges that this publication teaches various peptides from C3d. One of these peptides is P16 and is identical to human C3d residues 1217-1232 and has a length of 16 amino acids. Another one of these peptide is P10 is homologous to the human C3d residues at position 1217-1232 and has a length of 10 amino acids. Both of the P16 and P10 peptides are alleged to bind to CR2.

As for the Dawa reference, this reference does not predate the claimed priority of this application. The Examiner alleges that this reference teaches the adjuvant effect of C3d. The Examiner contends that "[c]omplement activation generates C3d which binds CR2 (CD21) on FDC, and B cells, thereby stimulating proliferation of B cells and generation of memory B cells and targeting antigen to the antigen presenting cell such as dendritic cells favor cell-mediated immunity."

Therefore, the Examiner concludes that it would have been obvious for one of ordinary skill in the art to substitute the C3d in the fusion protein of WO 96/17625 for the P16 or P10 peptide of Lambris "to target the fusion protein to the CR2 on B cells or dendritic cells as taught by Dawa et al.

The Examiner further alleges that one of ordinary skill in the art would be motivated to combined these references because when C3d binds to CR2 on FDC

and B cells, it stimulates the proliferation of Be cells and generation of memory B cells, and thus targets antigen to the antigen presenting dendritic cells as taught by Dawa et al.

Again, Applicant respectfully points out that independent claims have been amended to recite the elected species "wherein the antibody is specific for cellular receptor and the peptide is a specific binding site derived from a natural ligand for a specific cellular receptor; and wherein the antibody is a murine anti-idiotype antibody 3H1 and the peptide is a complement fragment C3d." Further, these independent claims have also amended to clarify that the peptide is a peptide of SEQ ID NO: 1.

Therefore, one of ordinary skill in the art would not be motivated to combined these references to make a fusion protein comprising comprising (1) an antibody and (2) a peptide of SEQ ID NO: 1; wherein the antibody is specific for cellular receptor and the peptide is a specific binding site derived from a natural ligand for a specific cellular receptor; and wherein the antibody is a murine anti-idiotype antibody 3H1 and the peptide is a complement fragment C3d.

Accordingly, Applicant respectfully submits it is not obvious for one of ordinary skill in the art to use the fusion protein of the WO 96/17625 document to make the claimed fusion protein because there is no teaching or suggestion in the WO 96/17625 document to make a fusion protein comprising a peptide of SEQ ID NO: 1, let alone an anti-binding fusion protein comprising an antibody and a peptide of SEQ ID NO: 1, having homophilic activity and has inverse hydrophathicity within the length of the peptide as recited in claimed invention.

Similarly, it is not obvious for one of ordinary skill in the art to substitute to substitute the C3d in the fusion protein of WO 96/17625 for the P16 or P10 peptide of Lambris "to target the fusion protein to the CR2 on B cells or dendritic cells as taught by Dawa et al.

Further, one of ordinary skill in the art would not be motivated to combined these references to make a fusion protein comprising a murine anti-idiotype antibody 3H1 and a peptide of SEQ ID NO. 1 that is a complement fragment C3d.

Applicant respectfully submits that one of ordinary skill in the art would have no motivation to combine these documents to make a fusion protein comprising a peptide of SEQ ID NO: 1 possessing homophilic activity let alone a peptide having inverse hydropathicity within the length of the peptide. There is no motivation for a skilled artisan to substitute or combine the peptide of WO 96/17625 with the peptide of Lambris et al. or Dawa et al. to make the claimed fusion protein.

In view of the above, Applicant respectfully submits that the Office Action has not made a prima facie case of obviousness. As such, the rejection of these claims under 35 USC §103(a), discussed above, should properly be withdrawn.

CONCLUSION

In light of the foregoing amendments and remarks, Applicant respectfully submits that the application is now in condition for allowance. Should any minor matter remain, or should the Examiner feel that an interview would expedite the prosecution of this application, the Examiner is invited to call the undersigned at his convenience.

To the extent necessary, Applicant petitions for an extension of time under 37 CFR 1.136. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to the Antonelli, Terry, Stout & Kraus, LLP Deposit Account No. 01-2135 (Docket No. 411.35629PC2), and please credit any excess fees to such Deposit Account.

Respectfully submitted,

ANTONELLI, TERRY, STOUT & KRAUS, LLP

By _____
Jessica H. Tran Bui
Reg. No. 40,846

JHB

1300 North Seventeenth Street, Suite 1800
Arlington, Virginia 22209
Telephone: (703) 312-6600
Facsimile: (703) 312-6666